

## REMARKS

### **Status of the Claims**

Claims 17-29 are currently pending. In the present Response, claims 18, 28, and 29 are amended. Thus, after entry of these amendments, claims 17-29 are presented for reconsideration.

Pursuant to the Office Action, claims 17-27 are rejected under 35 U.S.C. §112, first paragraph. Claims 18, 28, and 29 are rejected under 35 U.S.C. §112. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

### **Support for Claim Amendments**

Applicants respectfully request entry of the amendments set forth in the instant Response under 37 C.F.R. §1.116. The amendments place the case in condition for allowance and place the case in better condition for appeal; the amendments do not raise any issues of new matter; and the amended claims do not present new issues requiring further consideration or search.

Support for claim amendments can be found throughout the specification. In particular, support for amendments to claims 28 and 29 directed to a transaminase or aminotransferase activity wherein the activity is transferring an  $\alpha$ -amino group from an amino acid to an  $\alpha$ -ketoglutarate can be found at least at page 1, lines 14-16. The amendment to claim 18 clarifies the scope of the claimed invention. Applicants respectfully submit that no new matter is introduced by the instant amendments.

### **Issues under 35 U.S.C. §112, first paragraph**

Claims 17-27 are rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Patent Office alleges that transaminase or aminotransferase encompasses diverse enzymes having any substrate and stereo specificity. While the claims impart a structural limitation (70, 80, 90, or 95%), there is no specific functional limitation.<sup>1</sup> Thus, it is alleged that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants respectfully disagree. It should be noted that the level of knowledge and experience of the skilled artisan was very high at the time the application was filed. Thus, the skilled artisan would understand that transaminases or aminotransferases are enzymes that can catalyze the transfer of an amino group from an amino acid to an  $\alpha$ -keto acid. Moreover, the skilled artisan would understand that the enzymes will require an amino acid and an  $\alpha$ -keto acid as substrates, both of which the skilled artisan would recognize. The skilled artisan would also understand that to be an enzyme of the invention, structurally, it must be at least 70% identical to the amino acid sequences of SEQ ID NOS:25-32 and, functionally, it must have transaminase or aminotransferase activity.

To limit the claims to a specific transaminase or aminotransferase for specific substrates would provide too narrow a coverage and would allow potential infringers to use the teachings of the instant application to devise polynucleotides that encode an amino acid sequence related to SEQ ID NOS:25-32, but that have different donor or acceptor specificity. Like many, if not all enzymes, the aminotransferases of SEQ ID NOS:25-32 catalyze reactions to attain specific products from specific reactants. In other words, the catalytic reaction will be dependent on the specific reactants; however, the action/activity will remain the same. It would therefore, be onerous for the Applicants to list every possible reaction that the enzymes may catalyze and unnecessary for the skilled artisan to practice the claimed invention.

In previously issued claims, the Patent Office has not required claims to be limited to enzymes that performed a specific function as defined by the specific reactants and products. For example, U.S. Patent No. 6,416,984, claim 11 recites:

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<sup>1</sup> See page 2, line 21, to page 3, line 2, of the Office Action.

An isolated polypeptide comprising a first amino acid sequence 95% or more identical to a second amino acid sequence of amino acid residues 1 to 756 of SEQ ID NO:2 wherein said polypeptide has DNA mismatch repair activity.

These claims in the '984 patent and other similar claims are provided as Exhibits A-D. A more thorough search of the USPTO database will undoubtedly bring forth more claims where a polypeptide is claimed in terms of its activity, *e.g.*, DNA polymerase, without reference to a particular species of the enzymes having this activity or its specific substrates.

Therefore, Applicants respectfully submit that the written description requirement under 35 U.S.C. §112, first paragraph, should be no different for Applicants' enzyme than for similar claims directed to other enzymes, namely, requiring a structural limitation and a functional limitation related to the activity of the enzyme, as has been provided herein.

Based on the teachings of the instant disclosure, the skilled artisan would know that enzymes of the invention would have at least 70% identity to the amino acid sequences of SEQ ID NOS:25-32 and that the enzymes must have transaminase or aminotransferase activity. Accordingly, the claimed invention is described in terms of its structure and its function.

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Moreover, it is well within the knowledge of the skilled artisan to introduce mutations in proteins and to isolate DNA molecules (such as by library screening) encoding variant enzymes that fall within the scope of the claims. Once these variants are isolated, it is within the knowledge of the skilled artisan to identify those enzymes whose amino acid sequence is within the scope of the claimed invention (*e.g.*, at least 70% identical when aligned by BLASTN). It is also within the knowledge of the skilled artisan to identify those enzymes whose function is that of a transaminase or aminotransferase, such as transferring an  $\alpha$ -amino group from one amino acid to an  $\alpha$ -ketoglutarate, as acknowledged by the Patent Office on page 6, line 19, to page 20, line 1, of the Office Action. These activities would be a matter of routine experimentation (*e.g.*, sequencing the new clone and using the alignment program of BLASTN to measure percent identity and then using known methods to test the enzyme for its ability to transfer amino groups).

Regarding the difference between routine experimentation and undue experimentation, the Federal Circuit in *In re Wands* directed that the focus of the enablement inquiry to be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" is set forth by the Federal Circuit in, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*<sup>2</sup> An applicant had claims that were generic to all IgM antibodies directed to a specific antigen. However, only a single antibody producing cell line had been deposited.<sup>3</sup> The PTO had rejected claims that were generic to all antibodies directed to the antigen as lacking an enabling disclosure.

The Federal Circuit reversed, noting that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody species was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, it would not be undue experimentation to screen libraries or create mutations based upon the sequences taught in the instant specification to arrive at Applicants' claimed invention, as these protocols are well known, well accepted and practiced every day in research laboratories. Therefore, in light of the reasons provided above, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, as applied to claims 17-29.

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<sup>2</sup> *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987).

<sup>3</sup> The cell line was a hybridoma, thus, all of the antibodies it produced had the same structure and activity.

In the Patent Office's response to Applicants' arguments, it alleged "the genus of transaminases encompasses enzymes with widely different functions and because of that, a functional characteristic such as "transaminase activity is insufficient."<sup>4</sup>

Applicants aver that a limitation of Applicants' claimed invention is that the enzymes must have transaminase or aminotransferase activity. This activity (function) is described in the application as the transfer of an amino group from an amino acid to an  $\alpha$ -keto acid. In other words, all enzymes of the claimed invention must have transaminase or aminotransferase activity. Accordingly, Applicants respectfully submit that one skilled in the art would have appreciated the scope of the claimed invention.

With regard to the enablement argument, the Patent Office agrees that one of skill in the art would have known how to determine a specific defined transaminase activity, but disagrees with the notion that one skilled in the art would have known how to determine any possible transaminase or aminotransferase activity.<sup>5</sup> Applicants respectfully submit that one skilled in the art would have been able to determine the transaminase or aminotransferase activity of an enzyme, *i.e.*, transferring an amino group from an amino acid to an  $\alpha$ -keto acid, as exemplified by the transfer of an  $\alpha$ -amino group to the  $\alpha$ -carbon atom of  $\alpha$ -ketoglutarate as taught in the specification. Such assays were known in the art at the time the application was filed. Therefore, Applicants respectfully submit that instant claims sufficiently describe and enable one skilled in the art to practice the full scope of the claims. Applicants request reconsideration and withdrawal of the rejection of the claims based upon 35 U.S.C. §112, first paragraph.

#### **Issues under 35 U.S.C. §112, second paragraph**

Claims 18, 28, and 29 are rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

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<sup>4</sup> See page 6, lines 12-14, of the Office Action.

<sup>5</sup> See page 6, line 19, to page 7, line 7, of the Office Action.

Claim 18, line 4, recites "an enzyme encoded by an amino acid sequence." Applicants have amended claim 18 to recite "an enzyme having an amino acid sequence."

Claims 28 and 29 recite "enzyme has the same amino group acceptor and amino group donor specificity" without pointing out and distinctly claiming the amino group acceptor and donor. Applicants have amended these claims to more particularly claim the invention. Applicants have not changed the scope of the claims as the scope of the base claims 17 and 18 remain unchanged. Applicants have merely changed the focus of what is claimed to a particular transaminase/aminotransferase activity.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection based under 35 U.S.C. §112, second paragraph, as applied to claims 18, 28, and 29.

#### CONCLUSION

Claims 17-29 are pending in the application. Claims 18, 28, and 29 have been amended by the present Response. Applicants request that the Examiner reconsider the application and claims in light of the foregoing reasons and amendments and respectfully submit that the claims are in condition for allowance.

If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity to discuss any outstanding issues and to work with the Examiner toward placing the application in condition for allowance.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant : Patrick V. Warren et al.  
Serial No. : 09/389,537  
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Page : 9

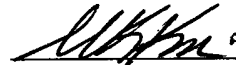
Attorney's Docket No.: 09010-017002

Applicants believe that no fees are necessitated by the present Response. However, in the event any fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

Respectfully submitted,

Date:

Sept 3, 2002



Mi K. Kim  
Reg. No. 44,830

Fish & Richardson P.C.  
4350 La Jolla Village Drive, Suite 500  
San Diego, California 92122  
Telephone: (858) 678-5070  
Facsimile: (858) 678-5099

**Version with markings to show changes made**

**In the claims:**

Claim 18, 28, and 29 have been amended as follows:

18. (Twice Amended) A method for transferring an amino group from an amino acid to an  $\alpha$ -keto acid comprising:

contacting an amino acid in the presence of an  $\alpha$ -keto acid with an isolated enzyme selected from the group consisting of an enzyme having [encoded by] an amino acid sequence which is at least 70% identical to any one of SEQ ID NOs:25-32 when aligned using the BLASTN program of the National Center for Biotechnology Information wherein the enzyme has transaminase or aminotransferase activity; and

thereby transferring an amino group from the amino acid to the  $\alpha$ -keto acid.

28. (Amended) The isolated enzyme of claim 17, wherein the transaminase or aminotransferase activity is an activity of transferring an  $\alpha$ -amino group from an amino acid to an  $\alpha$ -ketoglutarate [amino acid sequence of the isolated enzyme has the same amino group acceptor and amino group donor specificity as the enzyme to which it is at least 70% identical].

29. (Amended) The method of claim 18, wherein the transaminase or aminotransferase activity is an activity of transferring an amino group from an  $\alpha$ -amino acid to an  $\alpha$ -ketoglutarate [amino acid sequence of the isolated enzyme has the same amino group acceptor and amino group donor specificity as the enzyme to which it is at least 70% identical].



Applicant : Patrick V. Warren et al.  
Serial No. : 09/389,537  
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Attorney's Docket No.: 09010-017002

## **EXHIBIT A**

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**United States Patent**  
**Haseltine, et al.**

**6,416,984**  
**July 9, 2002**

## Human DNA mismatch repair proteins

### Abstract

The invention discloses three human DNA repair proteins and DNA (RNA) encoding such proteins and a procedure for producing such proteins by recombinant techniques. One of the human DNA repair proteins, hMLH1, has been mapped to chromosome 3 while hMLH2 has been mapped to chromosome 2 and hMLH3 has been mapped to chromosome 7. The polynucleotide sequences of the DNA repair proteins may be used for therapeutic and diagnostic treatments of a hereditary susceptibility to cancer.

Inventors: **Haseltine; William A.** (Washington, DC); **Ruben; Steven M.** (Olney, MD); **Wei; Ying-Fei** (Darnestown, MD); **Adams; Mark D.** (North Potomac, MD); **Fleischmann; Robert D.** (Gaithersburg, MD); **Fraser; Claire M.** (Potomac, MD); **Fuldner; Rebecca A.** (Barnesville, MD); **Kirkness; Ewen F.** (Olney, MD); **Rosen; Craig A.** (Laytonsville, MD)

Assignee: **Human Genome Sciences, Inc.** (Rockville, MD)

Appl. No.: **468024**

Filed: **June 6, 1995**

**Current U.S. Class:**

**435/183; 435/195**

**Intern'l Class:**

**C12N 009/00**

**Field of Search:**

**435/183,199 536/23.2,23.5**

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<u>6165713</u>	Dec., 2000	Liskay et al.	435/6.
<u>6191268</u>	Feb., 2001	Liskay et al.	436/23.

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*Primary Examiner:* Nashed; Nashaat T.

*Attorney, Agent or Firm:* Human Genome Sciences, Inc.

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***Parent Case Text***

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This application is a continuation-in-part of application Ser. No. 08/294,312 filed Aug. 23, 1994, which is a continuation-in-part of application Ser. No. 08/210,143 filed Mar. 16, 1994, which is a continuation-in-part of application Ser. No. 08/187,757 filed Jan. 27, 1994; and this application is also a continuation-in-part of PCT/US95/01035, filed Jan. 25, 1995. This application claims benefit of priority under 35 U.S.C. .sectn.120 of the four aforementioned applications.

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***Claims***

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What is claimed is:

1. An ***isolated*** polypeptide comprising an amino acid sequence of amino acid residues 1 to 756 of ***SEQ ID NO:2***.
2. The ***isolated*** polypeptide of claim 1 wherein said amino acid sequence comprises a heterologous polypeptide.
3. The ***isolated*** polypeptide of claim 1 which is glycosylated.
4. A composition comprising the ***isolated*** polypeptide of claim 1 and a carrier.
5. A polypeptide produced by a method comprising:
  - (a) culturing a host cell under conditions suitable to produce the ***isolated*** polypeptide of claim 1, wherein said host cell comprises a polynucleotide which encodes said polypeptide; and
  - (b) recovering the polypeptide.
6. An ***isolated*** polypeptide comprising the amino acid sequence of the full-length polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 75649.
7. The ***isolated*** polypeptide of claim 6 wherein said amino acid sequence comprises a heterologous polypeptide.
8. The ***isolated*** polypeptide of claim 6 which is glycosylated.
9. A composition comprising the ***isolated*** polypeptide of claim 6.

10. A polypeptide produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the *isolated* polypeptide of claim 6, wherein said host cell comprises a polynucleotide which encodes said polypeptide; and

(b) recovering the polypeptide.

11. An *isolated* polypeptide comprising a first amino acid sequence 95% or more identical to a second amino acid sequence of amino acid residues 1 to 756 of *SEQ ID NO:2* wherein said polypeptide has DNA mismatch repair *activity*.

12. The *isolated* polypeptide of claim 11 wherein said first amino acid sequence comprises a heterologous polypeptide.

13. The *isolated* polypeptide of claim 11 which is glycosylated.

14. A composition comprising the *isolated* polypeptide of claim 11 and a carrier.

15. A polypeptide produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the *isolated* polypeptide of claim 11, wherein said host cell comprises a polynucleotide which encodes said polypeptide; and

(b) recovering the polypeptide.

16. An *isolated* polypeptide comprising a first amino acid sequence 95% or more identical to the full-length polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 75649 wherein said polypeptide has DNA mismatch repair *activity*.

17. The *isolated* polypeptide of claim 16 wherein said first amino acid sequence comprises a heterologous polypeptide.

18. The *isolated* polypeptide of claim 16, which is glycosylated.

19. A composition comprising the *isolated* polypeptide of claim 16 and a carrier.

20. A polypeptide produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the *isolated* polypeptide of claim 16, wherein said host cell comprises a polynucleotide which encodes said polypeptide; and

(b) recovering the polypeptide.

21. An *isolated* polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence of amino acid residues 1 to 932 of *SEQ ID NO:4*; and

(b) an amino acid sequence of a fragment of *SEQ ID NO:4*, wherein the fragment has DNA mismatch repair *activity*.

22. The *isolated* polypeptide of claim 21 which comprises the amino acid sequence of (a).

23. The *isolated* polypeptide of claim 21 which comprises the amino acid sequence of (b).
24. The *isolated* polypeptide of claim 21 wherein said amino acid sequence comprises a heterologous polypeptide.
25. The *isolated* polypeptide of claim 21 which is glycosylated.
26. A composition comprising the *isolated* polypeptide of claim 21 and a carrier.
27. A polypeptide produced by a method comprising:
- (a) culturing a host cell under conditions suitable to produce the *isolated* polypeptide of claim 21, wherein said host cell comprises a polynucleotide which encodes said polypeptide; and
  - (b) recovering the polypeptide.
28. An *isolated* polypeptide comprising an amino acid sequence selected from the following:
- (a) an amino acid sequence of the full-length polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 75651; and
  - (b) an amino acid sequence of a fragment of the full-length polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 75651 wherein said fragment has DNA mismatch repair *activity*.
29. The *isolated* polypeptide of claim 28 which comprises the amino acid sequence of (a).
30. The *isolated* polypeptide of claim 28 which comprises the amino acid sequence of (b).
31. The *isolated* polypeptide of claim 28 wherein said amino acid sequence comprises a heterologous polypeptide.
32. The *isolated* polypeptide of claim 28 which is glycosylated.
33. A composition comprising the *isolated* polypeptide of claim 28 and a carrier.
34. A polypeptide produced by a method comprising:
- (a) culturing a host cell under conditions suitable to produce the *isolated* polypeptide of claim 28, wherein said host cell comprises a polynucleotide which encodes said polypeptide; and
  - (b) recovering the polypeptide.
35. An *isolated* polypeptide comprising a first amino acid sequence 95% or more identical to a second amino acid sequence selected from the group consisting of:
- (a) an amino acid sequence of amino acid residues 1 to 932 of *SEQ ID NO:4*; and
  - (b) an amino acid sequence of a fragment of *SEQ ID NO:4*, wherein the fragment has DNA mismatch repair *activity*;

and wherein said polypeptide has DNA mismatch repair *activity*.

36. The *isolated* polypeptide of claim 35 wherein said second amino acid sequence comprises (a).

37. The *isolated* polypeptide of claim 35 wherein said second amino acid sequence comprises (b).

38. The *isolated* polypeptide of claim 35 wherein said first amino acid sequence comprises a heterologous polypeptide.

39. The *isolated* polypeptide of claim 35 which is glycosylated.

40. A composition comprising the *isolated* polypeptide of claim 35 and a carrier.

41. A polypeptide produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the *isolated* polypeptide of claim 35, wherein said host cell comprises a polynucleotide which encodes said polypeptide; and

(b) recovering the polypeptide.

42. An *isolated* polypeptide comprising a first amino acid sequence 95% or more identical to a second amino acid sequence selected from the following:

(a) an amino acid sequence of the full-length polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 75651; and

(b) an amino acid sequence of a fragment of the full-length polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 75651 wherein said fragment has DNA mismatch repair *activity*;

and wherein said polypeptide has DNA mismatch repair *activity*.

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43. The *isolated* polypeptide of claim 42 wherein said second amino acid sequence comprises (a).

44. The *isolated* polypeptide of claim 42 wherein said second amino acid sequence comprises (b).

45. The *isolated* polypeptide of claim 42 wherein said first amino acid sequence comprises a heterologous polypeptide.

46. The *isolated* polypeptide of claim 42, which is glycosylated.

47. A composition comprising the *isolated* polypeptide of claim 42 and a carrier.

48. A polypeptide produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the *isolated* polypeptide of claim 42, wherein said host cell comprises a polynucleotide which encodes said polypeptide; and

(b) recovering the polypeptide.

Applicant : Patrick V. Warren et al.  
Serial No. : 09/389,537  
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Attorney's Docket No.: 09010-017002

## **EXHIBIT B**

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**United States Patent**  
**Danielsen , et al.**

**6,410,291**  
**June 25, 2002**

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**Polypeptides having haloperoxidase activity**

**Abstract**

The present invention relates to isolated polypeptides having haloperoxidase activity. The invention also relates to methods for producing and using the polypeptides.

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Inventors: **Danielsen; Steffen** (Copenhagen, DK); **Schneider; Palle** (Ballerup, DK)

Assignee: **Novozymes A/S** (Bagsvaerd, DK)

Appl. No.: **832498**

Filed: **April 11, 2001**

**Foreign Application Priority Data**

Apr 14, 2000[DK]

2000 00626

**Current U.S. Class:**

**435/192; 435/252.3; 435/320.1; 510/226; 530/300; 530/350;  
536/23.2**

**Intern'l Class:**

**C12N 009/08; C12N 001/20; C12N 015/00; C07H 021/04**

**Field of Search:**

**435/192,252.3,320.1 536/23.2 510/226 530/300,350**

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Oct., 1995

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Feb., 1997

WO.

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*Primary Examiner:* Saidha; Tekchand

*Attorney, Agent or Firm:* Lambiris; Elias

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**Parent Case Text**

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**CROSS-REFERENCE TO RELATED APPLICATIONS**

This application claims under 35 U.S.C. 119 priority from or the benefit of Danish application PA 2000

00626 filed Apr. 14, 2000 and U.S. application Ser. No. 60/202,249, filed May 5, 2000, the contents of which are fully incorporated herein by reference.

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### Claims

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What is claimed is:

1. An **isolated** polypeptide having haloperoxidase **activity**, selected from the group consisting of:
  - a) a polypeptide having an amino acid sequence which has at least 80% homology with the amino acid sequence of **SEQ ID NO:2**;
  - b) a polypeptide which is encoded by a nucleic acid sequence which hybridizes under medium stringency conditions with (i) the nucleotide sequence of **SEQ ID NO:1**, (ii) a subsequence of (i) of at least 100 contiguous nucleotides, or (iii) a full complementary strand of (i) or (ii).
2. The polypeptide of claim 1, having an amino acid sequence which has at least 95% homology with the amino acid sequence of **SEQ ID NO:2**.
3. The polypeptide of claim 1, comprising the amino acid sequence of **SEQ ID NO:2**.
4. The polypeptide of claim 1, consisting of the amino acid sequence of **SEQ ID NO:2** or a fragment thereof, having haloperoxidase **activity**.
5. The polypeptide of claim 4, consisting of the amino acid sequence of **SEQ ID NO:2**.
6. The polypeptide of claim 1, which is encoded by the nucleic acid sequence contained in the plasmid contained in *E. coli* DH10B, deposited as DSM 13442.
7. A method for producing the polypeptide of claim 1, comprising (a) cultivating a strain to produce a supernatant comprising the polypeptide; and (b) recovering the polypeptide.
8. A method for oxidizing a halide ion comprising reacting the halide ion and a source of hydrogen peroxide in the presence of the polypeptide of claim 1.
9. A method of halogenating a compound, comprising reacting the compound, a halide ion, and a source of hydrogen peroxide in the presence of the polypeptide of claim 1.
10. A method for killing microbial cells or inhibiting growth of microbial cells, comprising contacting the cells with the polypeptide of claim 1, a source of hydrogen peroxide, and a source of halide or thiocyanate in an aqueous solution.
11. A detergent composition, comprising a surfactant and the polypeptide of claim 1.

Applicant : Patrick V. Warren et al.  
Serial No. : 09/389,537  
Filed : September 2, 1999

Attorney's Docket No.: 09010-017002

## **EXHIBIT C**

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United States Patent  
Rey, et al.

6,432,898  
August 13, 2002

Polypeptides having lipase activity and nucleic acids encoding same

### Abstract

The present invention relates to isolated polypeptides having lipase activity and isolated nucleic acid sequences encoding the polypeptides. The invention also relates to nucleic acid constructs, vectors, and host cells comprising the nucleic acid sequences as well as methods for producing and using the polypeptides.

Inventors: **Rey; Michael W.** (Davis, CA); **Golightly; Elizabeth J.** (Davis, CA)

Assignee: **Novozymes Biotech, Inc.** (Davis, CA)

Appl. No.: **703416**

Filed: **October 31, 2000**

**Current U.S. Class:** 510/226; 435/196; 435/252.3; 435/320.1; 435/929; 536/23.2  
**Intern'l Class:** C12N 009/16; C12N 001/20; C12N 015/00; C07H 021/04  
**Field of Search:** 435/196,252.3,320.1,929 536/23.2 510/226

### References Cited [Referenced By]

#### Foreign Patent Documents

0869167	Dec., 1997	EP.
WO 98/26057	Jun., 1998	WO.

#### Other References

Sequence alignment of SEQ ID No : 1 & 2 With accession Nos. V07424 and W51767 disclosed in WO 98/26057.

*Primary Examiner:* Saidha; Tekchand  
*Attorney, Agent or Firm:* Starnes; Robert L.

### Claims

What is claimed is:

1. An isolated polypeptide having lipase *activity* obtained from *Fusarium venenatum*, selected from the group consisting of:

(a) a polypeptide having an amino acid sequence which has at least 90% identity with amino acids 31 to 349 SEQ ID NO:2;

(b) a polypeptide which is encoded by a nucleic acid sequence, wherein the nucleic acid sequence hybridizes under high stringency conditions with (i) nucleotides 1525 to 2530 of SEQ ID NO:1, (ii) the cDNA sequence contained in nucleotides 1525 to 2530 of SEQ ID NO:1, or (iii) a full complementary strand of (i) or (ii); and

(c) a fragment of (a) or (b), that has lipase *activity*.

2. The polypeptide of claim 1, having an amino acid sequence which has at least 95% identity with amino acids 31 to 349 of SEQ ID NO:2.

3. The polypeptide of claim 2, having an amino acid sequence which has at least 97% identity with amino acids 31 to 349 of SEQ ID NO:2.

4. The polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:2.

5. The polypeptide of claim 1, consisting of the amino acid sequence of SEQ ID NO:2 or a fragment thereof having lipase *activity*.

6. The polypeptide of claim 5, consisting of the amino acid sequence of SEQ ID NO:2.

7. The polypeptide of claim 6, which consists of amino acids 31 to 349 of SEQ ID NO:2.

8. The polypeptide of claim 1, which is encoded by a nucleic acid sequence, wherein the nucleic acid sequence hybridizes under high stringency conditions with (i) nucleotides 1525 to 2530 of SEQ ID NO:1 (ii) the cDNA sequence contained in nucleotides 1525 to 2530 of SEQ ID NO:1, or (iii) a full complementary strand of (i) or (ii).

9. The polypeptide of claim 1, which is encoded by a nucleic acid sequence, wherein the nucleic acid sequence hybridizes under very high stringency conditions with (i) nucleotides 1525 to 2530 of SEQ ID NO:1 (ii) the cDNA sequence contained in nucleotides 1525 to 2530 of SEQ ID NO:1, or (iii) a full complementary strand of (i) or (ii).

10. The polypeptide of claim 1, which is encoded by the nucleic acid sequence contained in plasmid pEJG60 which is contained in E. coli NRRL B-30333.

11. A method for producing the polypeptide of claim 1 comprising (a) cultivating a strain under conditions suitable for production of the polypeptide, wherein the polypeptide is native to the strain; and (b) recovering the polypeptide.

12. A detergent composition comprising a surfactant and the polypeptide of claim 1.

13. An isolated polypeptide having lipase *activity* comprising amino acids 31 to 349 of SEQ ID NO:2.

14. The polypeptide of claim 13, which is encoded by nucleotides 1525 to 2530 of SEQ ID NO:1.

Applicant : Patrick V. Warren et al.  
Serial No. : 09/389,537  
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## **EXHIBIT D**

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**United States Patent**  
**Andersen , et al.**

**6,429,000**  
**August 6, 2002**

## Pectin degrading enzymes from Bacillus licheniformis

### Abstract

Pectin degrading enzymes derived from or endogeneous to Bacillus licheniformis or other Bacillus species which are at least 99% homologous to Bacillus licheniformis based on aligned 16S rDNA sequences have optimum activity at pH higher than 8. The pectin degrading enzymes belongs to the enzyme classes pectate lyases (EC 4.2.2.2), pectin lyases (EC 4.2.2.10) and polygalacturonases (EC 3.2.1.15) and are useful in industrial processes under alkaline conditions such as in textile processing and as an active ingredient eg in laundry detergents and hard surface cleaning products.

Inventors: **Andersen; Lene Nonboe** (Aller.o slashed.d, DK); **Schulein; Martin** (Copenhagen, DK); **Lange; Niels Erik Krebs** (Raleigh, DK); **Bj.o slashed.rnvad; Mads Eskelund** (Frederiksberg, DK); **Schnorr; Kirk** (Copenhagen, DK)

Assignee: **Novozymes A/S** (Begsvaard, DK)

Appl. No.: **670141**

Filed: **September 26, 2000**

### Foreign Application Priority Data

Nov 24, 1997[DK]

1344/97

**Current U.S. Class:** **435/232; 435/200; 435/252.3; 435/252.33; 435/320.1; 536/23.2; 536/23.7**

**Intern'l Class:** **C12N.009/88; C07H.021/04**

**Field of Search:** **435/232,252.3,252.31,252.33,320.1,200 536/23.2,23.7**

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STN International, Chem. Abst. 118:250320.  
Derwent Accession No. 88-209811.  
EMBL, Database Genbank/DDBJ, Accession No. L416731.  
EMBL, GenBank/DDJ Accession No. D83791.

*Primary Examiner:* Nashed; Nashaat T.  
*Attorney, Agent or Firm:* Lambiris; Elias

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***Parent Case Text***

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This application is a continuation of U.S. application Ser. No. 09/198,956, filed Nov. 24, 1998, now U.S. Pat. No. 6,165,769, which is a continuation-in-part of U.S. patent application Ser. No. 09/073,684, filed on May 6, 1998 now U.S. Pat. No. 6,124,127. Also, this application claims priority under 35 U. S. C. 119 of Danish application 1344/97 filed Nov. 24, 1997, and benefit of U. S. Provisional application 60/067,240, filed Dec. 2, 1997.

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***Claims***

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What is claimed is:

1. An ***isolated*** polynucleotide molecule encoding a polypeptide having pectate lyase ***activity*** selected from the group consisting of:
  - (a) polynucleotide molecules comprising a nucleotide sequence of nucleotides 82-1026 of ***SEQ ID NO:*** 7;
  - (b) polynucleotide molecules that encode a polypeptide that is at least 90% identical to the amino acid sequence of residues 28-341 of ***SEQ ID NO:*** 8;
  - (c) polynucleotide molecules that hybridize with the nucleotide sequence of ***SEQ ID NO:*** 7 under hybridization conditions comprising 5.times.SSC at 45.degree. C. and washing conditions comprising 2.times.SSC at 60.degree. C.; and
  - (d) degenerate nucleotide sequences of (a), (b) or (c).
2. The polynucleotide molecule of claim 1, wherein the polynucleotide is DNA.
3. A polynucleotide molecule of claim 1, which comprises a nucleotide sequence of nucleotides 82-1026 of ***SEQ ID NO:*** 7.
4. A polynucleotide molecule of claim 1, which is a polynucleotide molecule that encodes a polypeptide that is at least 90% identical to the amino acid sequence of residues 28-341 of ***SEQ ID NO:*** 8.
5. A polynucleotide molecule of claim 1, which hybridizes with the nucleotide sequence of ***SEQ ID NO:*** 7 under hybridization conditions comprising 5.times.SSC at 45.degree. C. and washing conditions comprising 2.times.SSC at 60.degree. C.



6. An expression vector comprising the following operably linked elements: a transcription promoter; a polynucleotide molecule of claim 1 and a transcription terminator.
7. A cell comprising an expression vector of claim 6.
8. A method of producing a polypeptide having pectin degrading *activity*, comprising
  - (a) culturing a cell of claim 7; and
  - (b) recovering the polypeptide.